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INTER-OFFICE CORRESPONDENCE

PERSONAL &
CONFIDENTIAL

RICHMOND, VIRGINIA

[Handwritten signature]
[Handwritten initials]
Smoke Health
Trip Report

To: . Dr. R. B. Seligman
From: . T. S. Osdene
Subject: . European Trip Report

Date: June 15, 1977

MEETING WITH DR. D. G. FELTON, BAT, MAY 20, 1977

The first item on the discussion was the question of the stand by the HUNTER Committee on the subject of cocoa. It is to be remembered that they refused to allow cocoa to be added to any cigarette product. Felton understands that Fairweather, the Secretary of the HUNTER Committee, requires "A Life Time Inhalation Carcinogenesis Test Both in Rat and Hamsters" and further requires this testing both on added cocoa powder and probably chocolate as well as flavors derived from cocoa. Obviously, this seems to be an absurd demand and would entail a great deal of work. When questioned where this demand was made, Felton said that a letter stating this had been written to the Imperial Tobacco Co. Felton inquired about the United States Industry reaction to both the HUNTER decision and to the results reported by Gori. I felt that there was very little reaction. He also asked whether the Gori study would force any change in the industry--I felt that this was obviously open to further developments. When asked what BAT was going to do, Felton felt that probably a skin painting as well as the inhalation work would have to be done. However, he brought up the possible strategies which could be used:

1. Totally ignore the HUNTER Statement and simply carry on.
2. Do what has been requested by Fairweather. (Note that the possibility of obtaining unwanted results exist)
3. Perhaps the most exciting thing is to basically challenge HUNTER and his whole program and show him up for being somewhat nonsensical. Thus, for example, the lung cancer statistics of the U.S. versus the U.K. could be used to show where in the U.S. cocoa has been used for a long time and in the U.K. it hasn't. Nevertheless, the lung cancer incidence in the U.K. is far greater than that of the U.S.

We talked about a possibility, informally "whether one could cooperate with BAT in this endeavor." He felt that this would be quite possible and is in the process of preparing a white paper for BAT management. When asked whether he could conceivably do any

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of this work, he felt that probably Huntingdon Labs should be used. It should be pointed out that his own facilities at Southampton would not be large enough to conduct any of the work required. I asked if it would be possible to formally get Fairweather to make a statement on what and how he wishes to test cocoa, etc. Also, I had promised to inquire from Dr. Murray Senkus of R. J. Reynolds when meeting in Athens what his reactions were to the cocoa story (memo to file dated June 8, 1977). I agreed to call Felton on June 8 to discuss further what we might be able to do. Obviously, the question of response will have to be resolved at a higher level. In other discussions, it was mentioned that the Phase 4 of the HUNTER Protocol would probably cost between £500,000 and £800,000 per year for a period of probably 20 years. This would have to be undertaken for new products such as synthetics and probably would be done through the TAC.

The next subject was brought up by Dr. Felton who said that Ray Thornton, of BAT, was organizing a "Smoking Motivation and Behavior Conference" which would be basically run by BAT from the 27th of November to December 1 at Chelwood, England. He inquired whether Dr. Dunn could attend if invited and I said that this decision would have to be made in the United States. Part of the goals of this Conference would be to answer:

1. How low is "low in tar" and how far can you go before you extinguish smoking behavior?
2. Anything you can do with tobacco substitute we can do with tobacco.

Among those people who are going to be invited to the Conference are: Helmut Schievelbein of Germany, Stanley Schachter of the United States, as well as Fairweather and Hunter and select members of the United Kingdom industry. I understand that the number of people invited will be highly restricted due to space requirements, etc. In any case, I believe a formal invitation will be issued to Dunn.

Next we discussed the UNOR Analytical Device for NO which BAT has now marketed. It is a modified Luminox analyzer and several of these have been sold to Switzerland. Felton was of the opinion that this could also be used for nitrosamine determinations if one included a catalytic cracking device. The cost of the modified Luminox machine is approximately £4,000 or \$7,000 and Felton will send data on that device to me (now received).

We discussed some inhalation results which have been obtained at Southampton by Dr. Binns. The question was whether there was any reversion to normal within the larynx of a hamster or a rat after inhalation of smoke has ceased. They have found that all

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parameters return to normal within three weeks after cessation of smoking with the exception of the squamous metaplasia, which remained unchanged after 6 weeks. These data would correspond to that found in Germany.

I brought up the subject of the Royal College of Physicians report. This was done at the request of Mr. Don Hoel who contacted me in London. The official report will come out on June 2. However, Mr. Hoel has been successful in obtaining a copy of this earlier and since has mailed me a copy. Felton has written a critique of an earlier draft of the report and was waiting to see the final draft to be sure that his critique was still applicable. He stated further that before any press release was made he has been instructed to send a copy of his critique to Paul Isenring. This I communicated to Mr. Hoel. Felton doesn't expect TRC to make any formal critique what-so-ever but instead will keep a low profile.

Finally, there were two unrelated pieces of information:

1. BAT feels that it is possible that they may get a reversal for the ban of Coumarin in Germany. If this were true, this would mean that Coumarin would once again be allowed in Germany and may have greater implication for the use of Coumarin flavorants world-wide.
2. Dr. M. H. Russell will now definitely be joining Dr. Ernest Wynder in New York and will be leaving the United Kingdom shortly.

MEETING, NSM LIMITED AT FULSHAW HALL, ALDERLEY EDGE, CHESHIRE
ON MAY 23, 1977

Present at this meeting were Mr. Robert Hall, Dr. Colin Webster, Mr. Roger Reynolds and at lunch we were joined by Dr. David Conning. The following subjects were discussed:

Mr. Reynolds agreed that we may now divulge to Philip Morris Europe the NSM skin painting data which we have obtained. He will send us a letter confirming this. I expressed the opinion that we would be willing to at least repeat the test under question, namely that of 75% NSM in admixture with 25% of the U.S. tobacco blend. Reynolds and his coworkers felt that they had no alternative but to repeat this experiment since the data "would not go away" (it may be noted that large advertisements were placed in the English newspapers on Sunday the 29th of May and copies of this are attached.) As further discussion proceeded, it was decided that NSM would make a protocol proposal to us on additional skin painting which they deem desirable. We would then discuss this further and see if we can price

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it out. The outcome will be transmitted to Bob Hall. Discussions continued on how to conduct such an experiment, where to do it, and cost. Various possibilities included doing the complete experimentation in Germany in the INBIFO lab, in the United States, and perhaps also repeat the skin painting work at Alderley Edge under Dr. Conning's supervision. I did not feel that I should like to see this work done at Huntington Labs, U.K. No final decisions were made and we shall continue to exchange data to decide whether the experiment is worth doing. It seemed obvious that any decision would have to be made by the NSM Board and the people present were of the opinion that the Board may well decide to wait until they see the results of NSM in the market place. Discussions of cost sharing would then take place.

Mr. Reynolds stated that they have had a continuing dialogue with Gallaher and apparently Gallaher may well put NSM into one of their blends. Surprisingly, when questioned, he stated that Gallaher has given an indemnity and will indemnify NSM against any untoward effect. Mr. Reynolds then stated that NSM feels a moral obligation to inform Gallaher of the results of skin painting with NSM in a U.S. type blend. I have agreed that we should pose this question to our legal people for their opinion. It is my understanding that the agreement on the skin painting will run out toward the end of the year anyway, at which time NSM would be free to show the data to the third parties. Nevertheless, they should like to have our opinion on this and would obviously clean up the data so that no source can be traced to us. I asked the question, "IF this were made available to Gallaher would it then be made available to American Tobacco?" There was no real answer to this, but they were of the opinion that there was little or no communication between Gallaher, U.K. and American Tobacco.

There was some further discussion about the biology of NSM. Conning, in some short-term tests, seems to have found that it is possible that NSM may be a possible tumor initiator. They are repeating this test and it would seem very important to see the results of this. A general discussion on the value of short-term tests was discussed during lunch also and we were all of the opinion that one would have to wait and see of what value this was in the future. Overall, it was a cordial discussion and it seems obvious that NSM is now keen to push their material on the market. When asked what the basic reason was, they said, "Well, there was an implied health benefit." If one examines the new advertisement, one will see that this is indeed so.

MEETING WITH MR. DON HOEL, OF KANSAS CITY ON THE EVENING OF MAY 23, 1977, IN LONDON

Mr. Hoel and I discussed the possible implication of the new Royal College of Physicians' report which he felt was a very vital piece of information. It is my understanding that he will brief some of our top people at the oncoming meeting to be held in the U.K.

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Also, Mr. Hoel stated that there may be some opportunity at this time to influence some members of Parliament on both sides of the House, (i.e., labor and conservative). He was awaiting instructions on whether to proceed.

MEETING WITH MR. GLYN BURGAN, OF ITG, MAY 24, 1977, LONDON, ENGLAND

Mr. Glyn Burgan and I discussed final arrangements for the Pittsburg 4 conference and everything seems to be going well. The meeting will start on the morning of the 10th of September and finish on the evening of the 12th. On the probability of the success of synthetics in the United Kingdom Burgan was not terribly optimistic, but stated that sometime in July the first cigarettes containing NSM substitute would be out on the market. In general, it seems that the U.K. public has been exposed to much propaganda and, therefore, he felt that there may be a large initial interest in the substitutes.

MEETING WITH DR. KOENIG AND DR. ADLKOEFER - HAMBURG

A dinner meeting was held on May 26 in Cologne with Dr. Koenig and Dr. Adlkofer of Verband Der Cigarettenindustrie. This discussion was fairly generalized but they felt that the synthetic substances would not establish a foothold in Germany at this time. The only other subject of interest was the intense dislike shown about the visits of Mr. Ed Jacobs and Dr. Colby in Germany; however, they felt they had to be polite.

On Friday, May 27, I had a full-day meeting with Dr. Adlkofer and was joined at lunch time, also, by Dr. Bruckner. The subjects which we discussed were as follows:

Dr. Adlkofer, in his last visit to the United States, met with Dr. Bock of Roswell Park who gave him some data to be kept confidential about the cocarcinogenicity of nicotine (this is attached). The Germans feel that this is of vital importance and as a result have undertaken a study in which Dr. Grimmer and Dr. Bruner have denicotinized some condensate and reduced the level of nicotine in this from 4.6% down to 0.2% of nicotine. They will then add nicotine to this condensate and do skin painting to see what effect, if any, nicotine has as a cocarcinogen. He briefly showed me the experimental design for the denicotinization and I must confess I believe that other nitrogen containing basic materials will also be removed. Nevertheless, one should keep an eye open for the results of this--perhaps Dr. Hausermann can supply us the data as it develops. Dr. Adlkofer confirmed that Russell is definitely going to join Wynder and will permanently leave the United Kingdom.

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We discussed the recently published paper on the Legionnaires Disease (re. nickel) appearing in Science Vol. 196, May 20, 1977. Apparently there is still some interest by someone in the Health Office in Berlin on this subject and I pointed out that there seem to have been shown unequivocally that the Legionnaires Disease has been caused by bacterial causes. Adlkofer further mentioned that a man in Berlin was still extremely keen on the subject of halogenated hydrocarbons and their potential danger in smoke. Thus, they still are concerned about the generation of phosgene in smoke. It seems absurd to consider this seriously since chemically it is most improbable. Adlkofer doesn't consider this a threat but he says that it is still under consideration in Germany. Further, we had a discussion on the various short-term tests including the Ames Test and he again mentioned that Sugimura in Tokyo had shown that certain of the harmanes and nor-harmanes are approximately 10,000 times as potent as BAP--this should be examined further. He had some questions regarding Dr. Georg Neurath and mentioned the possibility that he may get a contract for the monitoring of exhaled NO. Finally, there was an informal discussion on Hackenberg. It would appear that Adlkofer is about to go to his Board to obtain permission to do a 1.5 million DM experiment jointly between Hackenberg and Altman in Vienna. This would involve studies on the DNA repair mechanism using tobacco condensates. Dr. Hackenberg did not mention this to me previously.

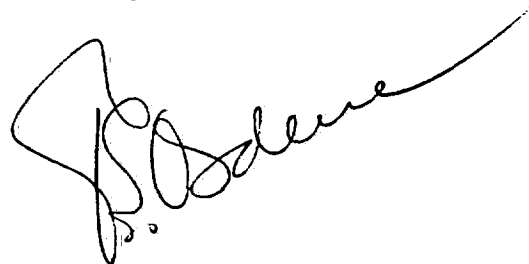
At lunch that day we met Dr. Brucker, who is the Legal Head of the Verband Der Cigarettenindustrie. I brought up the subject of Paragraph 20 in the German Food Laws and he gave me some kind of an explanation thereof. It would appear that smoke cannot be considered a natural product in the terms of the ordinance since it is not found directly in leaf tobacco, although, of course it is derived from it. There are certain legalistic questions regarding to the interpretation of these articles and both the quantitative aspects and the definition of raw tobacco, whether this is green or cured, are still under discussions. Anyway, we shall keep a close eye since this may well affect the German Food Laws in the future. One can, however, use leaf tobacco as a natural source or its chemical equivalent in any flavor questions. Apparently, there seems to be no high probability that at this time testing of new materials obtained from these sources will have to be undertaken.

Over the weekend I had several discussions with Dr. Neurath on the subject of nitrosamine and also about the Thermoelectron Corp. Analyzer which he considers to be an excellent one. It is my recommendation that we go ahead and purchase one. Dr. Neurath informed me that there will be a meeting on nitrosamines sometime in the latter part of August in New Hampshire and I would suggest that if we can get details and get someone to go to the meeting

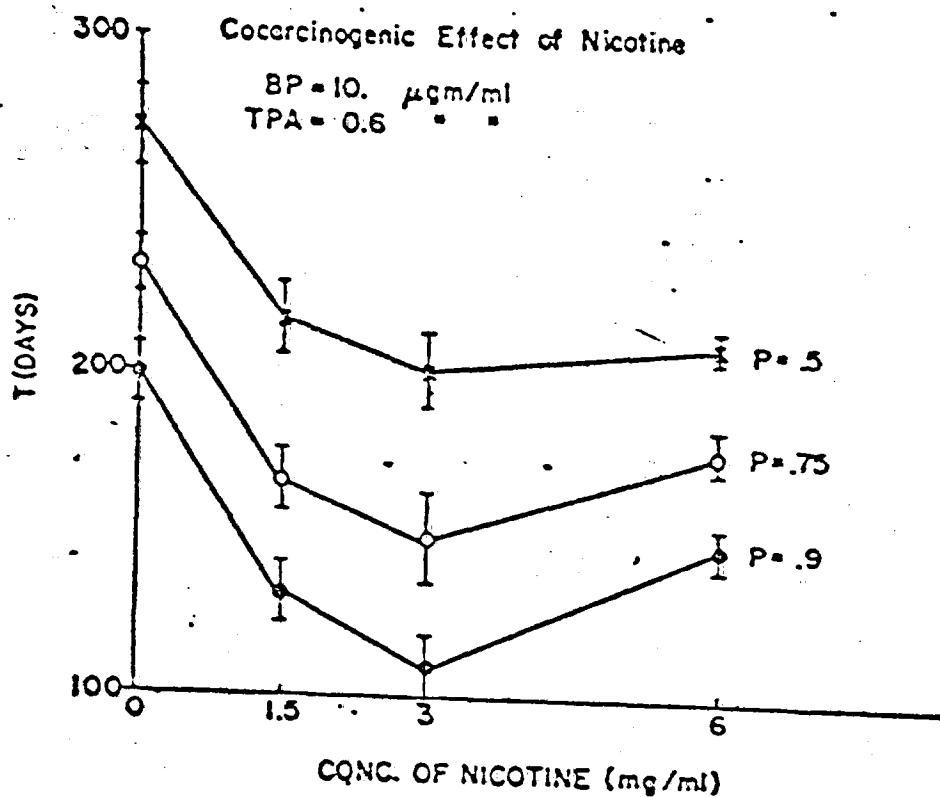
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this would be worthwhile (Dr. Einolf will attend). Apparently, there still seems to be quite a great deal of interest on nitrosamines per se. Dr. Hoffmann et al. will also be attending this meeting. Dr. Neurath did not mention any of the work which may be conducted with the Verband Der Cigarettenindustrie and I did not bring this up any further.

TSO/mro

A handwritten signature in black ink, appearing to be "B. Osden", written in a cursive style.

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Figs. 2-4 { mixtures of Benzo[a]pyrene } in acetone
 + 7 { TPA
 Nicotine }

Painted on ICR Swiss mice 0.2 ml 10x weekly
 Data refers to total tumor incidence (corrected
 for competing causes of death)

Fig. 2. Time required for 10% ($P=0.9$)
 25% ($P=0.75$) or
 50% ($P=0.5$) of the
 mice to develop tumors \pm standard error
 (estimated from maximum likelihood fit
 to Weibull curve).

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Patrick Proisy, the joint French No. 2, as the sun was setting over the Stade Roland Garros.

Linda's performance was the more convincing. She always had too many big shots for the slender Miss Mayer, who is ranked 13th in the United States.

Buster, the 22-year-old loner who has reached the semi-finals of his last two tournaments—in Hamburg and Dusseldorf—had more problems with Proisy, an agile retriever who seemed to cover many of Mottram's volleys even before they were struck.

Mottram in the second round of the women's singles with a 6-4, 6-4 win over another American, Mary Hamm, but Jackie Fayter, after trailing 5-0 and fighting back 5-5 in the first set, collapsed to a 7-5, 6-1 defeat against tiny South African Linkie Boshoff.

Ilie Nastase, playing too nonchalantly for comfort, was taken to five sets by 25-year-old American Tim Guilikson before winning 6-3, 3-6, 4-6, 6-2, 6-1.

Eddie Digbs, the fourth seed, was not so fortunate. He went out 6-3, 3-6, 7-5, 6-4, to Rolf Warberg, of Sweden.

pression.

Closest to them going into today's third round are Tony Jacklin and Spain's diminutive Manuel Pinero — trailing by three shots.

● The 18-hole final of the English women's championship at Burnham and Berrow will be an all Yorkshire clash between Mary Everard, who beat Angela Uzcili 5 and 3 in the semi-final, and Vanessa Marvin, who beat Beverly Huke 3 and 1.

Today's fixtures

GOLF.—Penfold PGA Championship, Sandwich—English Women's Championship, Burnham & Berrow.
LAWN TENNIS.—Surrey Championship, Surbiton L.T.C., Bettylands, Surbiton

SHOW JUMPING.—Tidworth Horse Trials, Tidworth, Hants.

SPEEDWAY.—Gull British League: Hackney v Cradley (8)—Wolverhampton v Hull (7.30). National League: Cambridge v Workington (7.30). K.E. Cup: Edinburgh v Sloke (7.30) K.R.C. Trophy: Peterboro (7.30) Challenge Match: Bristol v I Manger's Select (7.30).

YACHTING.—Weymouth Olympic Regatta.

able to disrupt the whole German defence, constantly leading Vogts on a wild goose chase.

Europe pays its tribute

PICTURE BY JOHN DAWES

ENZO BEARZOT, Italy's manager who aims to stop England reaching the World Cup finals in the Argentine, yesterday led the European fanfares for Liverpool.

"Who said that English football was on the wain," he asked after Liverpool had swamped Borussia Moenchengladbach, to win the European Cup.

"Liverpool fully deserved to win. Keegan was too tough a bone for Vogts to chew."

The Italian Press—not noted for their love of English teams—agreed.

Il Giornale said: "The Lions

By Malcolm Folley

of Liverpool are born again. They won so convincingly as to give Borussia no excuse.

Il Giornale, also of Milan, commented: "Liverpool kept constantly on the attack when possibly most Italian sides would have gone on to the defence once in the lead."

Turin's La Stampa said: "Liverpool dominated the game. They were led by Keegan in exceptionally brilliant form."

It was bad news for the Italy team, but Don Revie will probably help by fielding a disjointed England side in November."

West Germany's Die Welt said: "The decisive factor was that Borussia's cover proved far weaker than usual and that only Simonsen was sharp in attack. For Liverpool Keegan was most impressive."

Liverpool's victory was heralded in France. France Soir said: "They are worthy successors to Bayern."

Le Figaro added: "Magic Liverpool."

There was a similar story in Spain, where a Real Madrid official said: "Liverpool are splendid champions of Europe. The team hardly put a foot wrong throughout the match."



FROM ROTHMANS INTERNATIONAL

PEER



The world's first cigarette with Cytrel tobacco substitute



This brand is designed to be LOW TAR GROUP As defined in I.M. Government Tables.

EVERY PACKET CARRIES A GOVERNMENT HEALTH WARNING

L6E6ZLE001

What every cigarette smoker should know about NSM.

A new standard in tobacco substitutes.

NSM* is a totally new concept in tobacco substitutes.
NSM has been developed following an extensive research programme over many years, financed jointly by Imperial Tobacco and ICI.

The objective in developing NSM has been to convert natural plant material into a form which might help to reduce the risks which medical authorities have associated with cigarette smoking.

A programme of laboratory research has been completed to the satisfaction of the Independent Scientific Committee on Smoking and Health[□] which has agreed to the use of NSM in certain cigarette brands. [□]The Hunter Committee, appointed by H.M. Government.

Research has shown that when NSM burns, it produces smoke which is different in both its nature and its effects from that produced by Virginia tobacco:

- 1. NSM produces less than one-third as much tar.**
- 2. NSM produces not just less tar but tar which is about one-third as biologically active** (when measured by a standard mouse skin painting technique).
- 3. NSM produces a less irritant smoke.**

The extent to which these attributes of NSM are effective in a product made from a blend of NSM with Virginia tobacco will depend on the specification of the cigarette and the proportion of NSM and tobacco in the blend.

Cigarettes containing NSM tobacco substitute will be available in July.



Issued by New Smoking Materials Limited

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